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Et al.

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COLLABORATING TO CURE THE MOST COMMON PARASITES ON THE PLANET

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Soil-transmitted helminths (STHs), most notably, hookworms, whipworms, and *Ascaris*, are nematodes that infect more than 1.5 billion of the poorest people and are leading causes of morbidity worldwide. Only one class of de-worming drugs (anthelmintic) is commonly used in mass drug administrations. New anthelmintics are urgently needed to overcome emerging resistance and to produce higher cure rates. Crystal (Cry) proteins, in particular Cry5B, made by *Bacillus thuringiensis* (*Bt*) are promising new candidates. Cry5B has excellent anthelmintic properties against many free-living and parasitic nematodes, including *in vivo* efficacy against multiple STH infections in rodents (*Heligomasmidoes polygyrus* and *Ancylostoma ceylanicum*) and in pigs (*Ascaris suum*).

An enormous challenge for STHs, very different from most diseases worked on in the developing world, is the requirement that therapies be very cheap (the people infected are very poor and current drugs costs pennies a dose), massively scalable (over 4 billion people are at risk from infection), and have a long shelf life in harsh environments, that have high temperature and humidity and no cold chain.

Working together, we have made excellent progress in our development efforts to produce a deployable version of Cry5B that is cheap, safe, scalable, and stable. These efforts are focused on microbiology, bacterial engineering, expression, and formulation. In the process of this work, we have discovered a novel bacterial expression system that meets these key requirements. In addition, we will provide latest information about the broad spectrum of activity of Cry5B against key parasites that make this therapeutic a very attractive alternative from current treatments.

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